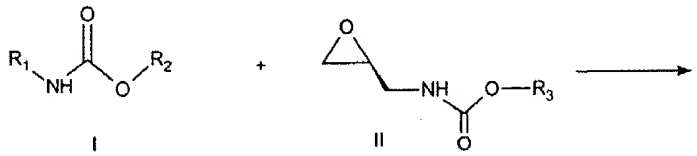
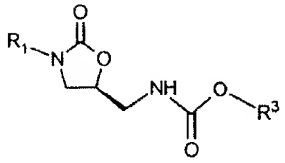
-- The present invention is directed to a method of synthesizing oxazolidinones and intermediate compounds used in the synthesis. As shown in Schemes 1, 2, and 3 below, one aspect of the present invention is to provide an

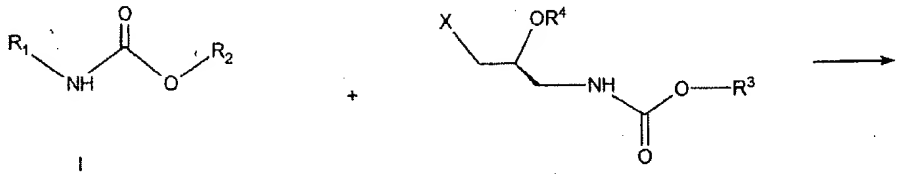
Scheme 1



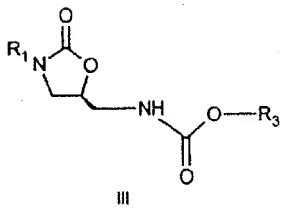
I II



Scheme 2

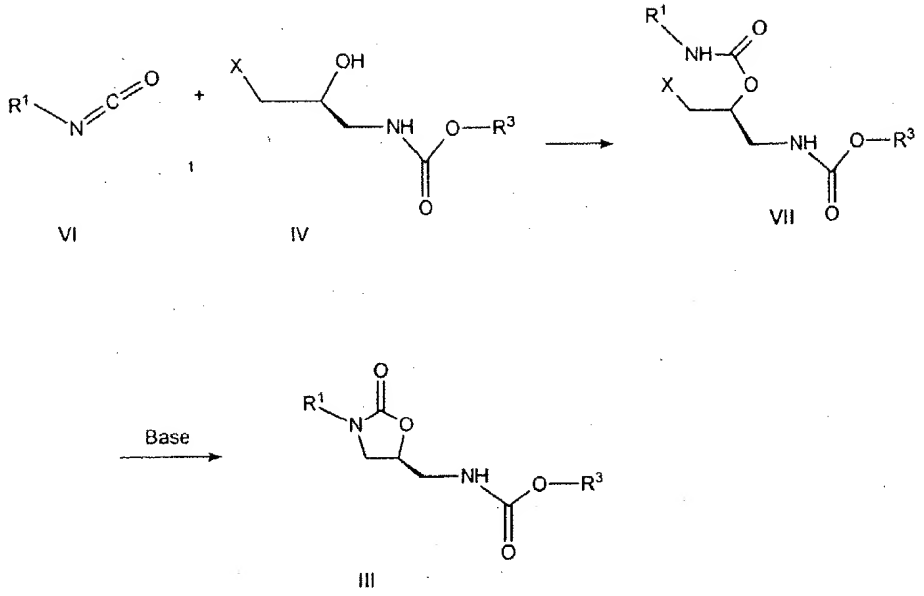


I IV, R^4 = H
V, R^4 = C_1-C_6 alkylcarbonyl



III

Scheme 3

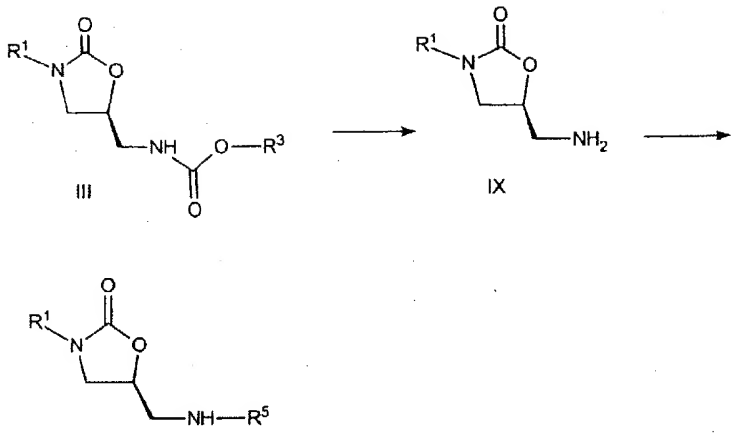


S)-oxazolidinone alkylcarbamoyl intermediate of structural formula (III), an (S)-secondary alcohol of structural formula (IV), and an (S)-ester/protected alcohol of structural formula (V), or a salt or hydrate thereof or acceptable salts, hydrates, or pro-compounds thereof, wherein R^1 is optionally substituted aryl; R^2 is selected from the group consisting of C_1-C_{20} alkyl, C_3-C_7 cycloalkyl, aryl optionally substituted with one or two C_1-C_3 alkyl or halogen groups, allyl, 3-methylallyl, 3,3-dimethylallyl, vinyl, styrylmethyl, benzyl optionally substituted on the aryl with one or two Cl, C_1-C_4 alkyl, nitro, cyano, or trifluoromethyl groups, 9-fluorenylmethyl, trichloromethylmethyl, 2-trimethylsilylethyl, phenylethyl, 1-adamantyl, diphenylmethyl, 1,1-dimethylpropargyl, 2-furanylmethyl, isobornyl, and hydrogen; R^3 is C_1-C_{10} alkyl; R^4 is H or C_1-C_5 alkylcarbonyl; and X is halogen, alkylsulfonyloxy, or arylsulfonyloxy. --

Please replace the paragraph beginning at page 11, line 16, with the following amended paragraph:

-- An additional aspect of the present invention, as shown in Scheme 7, is

Scheme 7



X, R^5 = C_1-C_6 alkylcarbonyl or C_1-C_6 cycloalkylcarbonyl
XI, R^5 = C_1-C_6 alkylthiocarbonyl or C_1-C_6 cycloalkylthiocarbonyl

to provide a process for the production of an (S)-3,5-disubstituted-oxazolidinone of the structural formula (X) and (XI) which comprises (a) contacting a carbamate of structural formula (I) with an (S)-protected alcohol of formula (V) in the presence of a lithium cation and a base whose conjugate acid has a pKa of greater than about 8 to provide an (S)-protected-oxazolidinone of the structural formula (III) (see Scheme 2), (b) contacting the reaction product of step (a) with aqueous acid to produce an (S)-oxazolidinone free amine of structural formula (IX), and (c) contacting the product of step (b) with a base, such as a tri(C_1-C_5 alkyl)amine, and an acylating or thioacylating agent selected from the group consisting of (i) an acid anhydride of the structural formula $O(R^5)_2$, (ii) an activated acid of the structural formula R^5X to provide (X) or (iii) a dithioester of the structural formula $R^5S(C=S)R^5$ to provide (XI), wherein R^5 is C_1-C_6 alkylcarbonyl, C_1-C_6 cycloalkylcarbonyl, C_1-C_6 alkylthiocarbonyl, or C_1-C_6 cycloalkylthiocarbonyl, and X is halogen, alkylsulfonyloxy, or arylsulfonyloxy. --

Please replace the paragraph beginning at page 13, line 4, with the following amended paragraph:

-- A further aspect of the present invention is to provide a one pot process for the production of an (S)-oxazolidinone of structural formula (X) and (XI) which comprises (a) contacting a carbamate of formula (I) with either an (S)-t-butylcarbamyl secondary alcohol of the structural formula (IV) or an (S)-t-butylcarbamyl epoxide of the structural formula (II), in

the presence of a lithium cation and a base whose conjugate acid has a pKa of greater than about 8, (b) contacting the product of step (a) with aqueous acid, and (c) contacting the reaction product of step (b) with a base, such as a tri(C_1-C_5 alkyl)amine, and and an acylating or thioacylating agent selected from the group consisting of (i) an acid anhydride of the structural formula $O(R^5)_2$, (ii) an activated acid of the structural formula R^5X, or (iii) a dithioester of the structural formula $R^5S(C=S)R^5$, wherein R^5 is C_1-C_6 alkylcarbonyl, C_1-C_6 cycloalkylcarbonyl, C_1-C_6 alkylthiocarbonyl, or C_1-C_6 cycloalkylthiocarbonyl, and X is halogen, alkylsulfonyloxy, or arylsulfonyloxy. --

Please replace the paragraph beginning at page 14, line 16, with the following amended paragraph:

-- The term "alkylsulfonyloxy " is defined as R-SO_3-, where R is alkyl. --

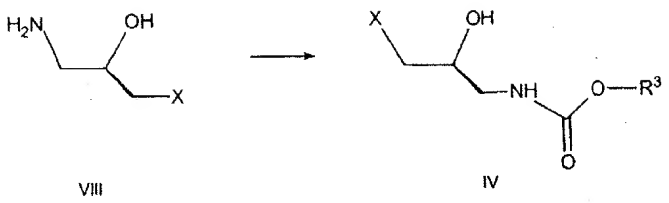
Please replace the paragraph beginning at page 14, line 17, with the following amended paragraph:

-- The term "arylsulfonyloxy " is defined as R-SO_3-, where R is aryl. --

Please replace the paragraph beginning at page 21, line 14, with the following amended paragraph:

-- The three carbon nitrogen containing fragments, i.e., (S)-secondary alcohol (IV), (S)-epoxide (II), and (S)-ester (V), can be produced by different routes, as illustrated in Schemes 4, 5, and 6. Scheme 4 illustrates a process of preparing a

Scheme 4



VIII IV

(S)-3-carbon amino alcohol (IV) from an (S)-amino alcohol (VIII) and a dialkyldicarbonate. For the (S)-amino alcohol (VIII), X can be halogen, alkylsulfonyloxy, or arylsulfonyloxy. A preferred X is Cl. The (S)-amino alcohols (VIII) are known to those skilled in the art or can readily be prepared from known compounds by methods disclosed in WO 99/24393 from commercially available S-epichlorohydrin. The (S)-amino alcohol can be isolated in crystalline form after recrystallization. The reaction of dialkyldicarbonate and the (S)-amino alcohol (VIII) is performed as set forth in Example 3. --

Please replace the paragraph beginning at page 23, line 1, with the following amended paragraph:

-- Scheme 5 illustrates a process for converting an (S)-carbamoyl alcohol

Scheme 5

IV V, R^4 = C_1-C_6 alkylcarbonyl

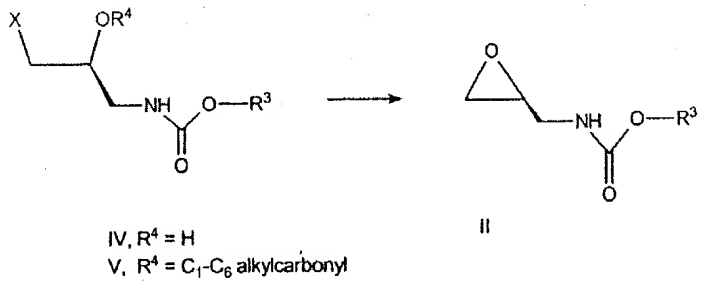
(IV) to a corresponding (S)-secondary ester/protected alcohol (V). To convert an (S)-carbamoyl alcohol (IV) to a corresponding (S)-secondary ester/protected alcohol (V), the (S)-carbamoyl alcohol (IV) is reacted with an appropriate acylating reagent, such as an acyl halide or acyl anhydride, under acylation reaction conditions well known to those skilled in the art. The (S)-secondary protected-alcohol can be isolated in crystalline form after recrystallization. For example, an (S)-carbamoyl alcohol (IV) can be transformed to a

corresponding (S)-secondary ester/protected alcohol (V) by reaction with acetic anhydride in triethylamine, as is set forth in Example 4. For the (S)-3-carbon amino alcohol (IV), X can be halogen, alkylsulfonyloxy, or arylsulfonyloxy, and preferably is Cl. For the corresponding corresponding (S)-secondary ester/protected alcohol (V), R^4 is C_1-C_5 alkylcarbonyl and preferably is acetyl. It is preferred that the acylating reagent be selected from the group consisting of an acid anhydride of the formula $O(R^5)_2$, wherein R^5 is C_1-C_6 alkylcarbonyl, or an activated acid of the formula R^5 X, wherein X can be halogen, alkylsulfonyloxy or arylsulfonyloxy and preferably is -Cl or -Br, and used in conjunction with base, preferably a tri(C_1-C_5 alkyl)amine. It is more preferred that R^5 is acetyl and X is -Cl. Specifically, the more preferred acylating reagent is an acyl anhydride, and it is most preferred that the acyl anhydride is acetic anhydride. --

Please replace the paragraph beginning at page 23, line 25, with the following amended paragraph:

-- Scheme 6 shows a process of preparing a (S)-epoxide (II) from either

Scheme 6



IV, R^4 = H
V, R^4 = C_1-C_6 alkylcarbonyl

II

an (S)-3-carbon amino alcohol (IV) or an (S)-secondary ester/protected alcohol (V). The (S)-epoxide (II) can be obtained by reaction of an (S)-secondary ester/protected alcohol (V) with a base, such as potassium or lithium t-butoxide, in a solvent, such as methanol. The (S)-epoxide can be isolated in crystalline form after chromatography. An (S)-epoxide (II) can be produced from a corresponding (S)-secondary alcohol (IV) by reaction with lithium t-butoxide in methanol at 20°C, as is set forth in Example 5. For an (S)-secondary alcohol (IV) or (S)-secondary ester/protected alcohol (V), it is preferred that R^4 is acetyl. For either an

(S)-3-carbon amino alcohol (IV) or (S)-secondary ester/protected alcohol (V), X can be halogen, alkylsulfonyloxy, or arylsulfonyloxy, and preferably is Cl. --

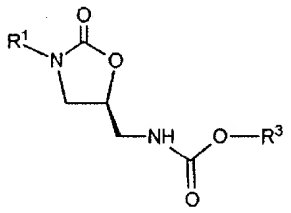
Please replace the paragraph beginning at page 25, line 10, with the following amended paragraph:

-- Alternatively, the transformation from compound (III) to compound (X) or (XI) can be accomplished as a one pot process without isolating amine (IX). It is preferred that the acylating or thioacylating agent is selected from the group consisting of an acid anhydride of the structural formula $O(R^5)_2$, an activated acid of the structural formula R^5X, and a dithioester of the structural formula $R^5S(C=S)R^5$, wherein R^5 is C_1-C_6 alkylcarbonyl, C_1-C_6 cycloalkylcarbonyl, C_1-C_6 alkylthio-carbonyl, or C_1-C_6 cycloalkylthiocarbonyl, and X is halogen, alkylsulfonyloxy, or arylsulfonyloxy. It is preferred that the acylating agent or thioacylating agent is used in conjunction with a base, such as a tri(C_1-C_5 alkyl)amine. It is more preferred that R^5 is acetyl and X is Cl. Specifically, it is more preferred that the acylating reagent is an acyl anhydride, and most preferably the acyl anhydride is acetic anhydride. --

In the Claims:

Please replace claims 17, 32, and 57-58 with the following amended claims:

17. (Amended) An (S)-intermediate having a general structural formula:



wherein R^1 is an substituted aryl group and R^3 is C_1-C_{10} alkyl, or a salt or hydrate thereof, provided that when R^3 is C_1-C_4 alkyl or C_7-C_{11} araalkyl and R^1 is phenyl, the substituents on R^1 are not hydrogen, monofluoro, monochloro, monobromo, or mononitro